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| 09/980,954      | 02/15/2002  | Akira Kaji           | K0448/7012          | 3440             |

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EXAMINER

STEADMAN, DAVID J

ART UNIT PAPER NUMBER

1652

DATE MAILED: 06/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/980,954

Applicant(s)

KAJI ET AL.

Examiner

David J. Steadman

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 2/18/05, 3/7/05, and 5/2/05.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1 and 52-59 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 52-59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 2/18/05, 3/12/02.

- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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**DETAILED ACTION**

***Status of the Application***

- [1]** Claims 1 and 52-59 are pending in the application.
- [2]** Applicants' amendment to the claims, filed 2/18/2005, and supplemental amendment to the claims, filed 3/7/2005, are acknowledged. The listing of the claims filed 3/7/2005 replaces all prior versions and listings of the claims.
- [3]** Applicants' amendment to the specification, filed 2/18/2005, is acknowledged. This amendment fails to meet the requirements of 37 CFR 1.121 for the reason(s) set forth in the Office communication mailed 3/29/2005.
- [4]** Applicants' amendment to the specification, filed 5/2/2005, is acknowledged. This amendment corrects the deficiencies of the amendment filed 2/18/2005.
- [5]** Receipt of an information disclosure statement, filed 2/18/2005, is acknowledged.
- [6]** Receipt of an English language translation of the foreign priority document, filed 3/7/2005, is acknowledged.
- [7]** Applicants' remarks/arguments filed on 2/18/2005, 3/7/2005, and 5/2/2005 have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [8]** The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

***Information Disclosure Statement***

[9] All references cited in the information disclosure statement (IDS) filed 2/18/2005 have been considered by the examiner. A copy of Form PTO-1449 is attached to the instant Office action.

[10] As noted in a previous Office action, reference C7 of the IDS filed 3/12/2002 was not considered by the examiner as the reference could not be located in the application. In the amendment filed 3/7/2005, applicants have provided the reference and it has been considered. A copy of Form PTO-1449 is attached to the instant Office action.

#### ***Claim for Foreign Priority***

[11] Applicants' claim for foreign priority under 35 USC 119(a)-(d) to Japanese application 11-158637, filed June 04, 1999, is acknowledged. It is noted that June 04, 2000 falls on a Sunday, while June 05, 2000 falls on a Monday, thus the claim is considered valid. A certified copy of the foreign priority document and an English language translation thereof have been filed in the instant application, thus perfecting the priority claim.

#### ***Specification/Informalities***

[12] The objection to the specification (§ 7] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to the specification filed 5/2/2005. The reference to Table 7 as providing the structural coordinates of RRF (e.g., p. 23, bottom, of the specification) has been amended to refer to Table 8.

***Claim Objections***

**[13]** The objection to claims 1-8, 12-14, 16-17, and 19-22 in the recitation of "RRF" (§ [8] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to claim 1 to recite the entire phrase, *i.e.*, "ribosomal recycling factor" for which the abbreviation "RRF" is used.

**[14]** MPEP 2173.02 states, "if the language used by applicant satisfies the statutory requirements of 35 U.S.C. 112, second paragraph, but the examiner merely wants the applicant to improve the clarity or precision of the language used, the claim must not be rejected under 35 U.S.C. 112, second paragraph, rather, the examiner should suggest improved language to the applicant." In this case, claim 1 is objected to as active method step a), with the exception of defining the three-dimensional structure, is essentially repeated in active method step b). It is suggested that applicants incorporate the two active method steps into a single active method step, e.g., employing said three-dimensional structure of said protein as defined by the atomic coordinates of RRF protein according to Table 8 to design or select said compound capable of binding to RRF protein.

***Claim Rejections - 35 USC § 112, Second Paragraph***

**[15]** The rejection of claim 1 (claims 2-8, 12-17, and 19-22 rejected as being dependent therefrom) as being indefinite for not setting forth any method steps (§ [9] part [a] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to claim 1 and cancellation of claims 2-8, 12-17, and 19-22.

**[16]** The rejection of claim 1 (claims 2-8, 12-17, and 19-22 rejected as being dependent therefrom) as being indefinite in the recitation of "active site, an accessory binding site or a pocket of an RRF protein" (§ [9] part [b] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to claim 1 and cancellation of claims 2-8, 12-17, and 19-22.

**[17]** The rejection of claim 1 (claims 2-8, 12-17, and 19-22 rejected as being dependent therefrom) as being indefinite in the recitation of "computationally evaluating" (§ [9] part [c] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to claim 1 and cancellation of claims 2-8, 12-17, and 19-22.

**[18]** The rejection of claim 1 (claims 2-8, 12-17, and 19-22 rejected as being dependent therefrom) as being indefinite in the recitation of "a chemical entity of RRF protein" (§ [9] part [d] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to claim 1 and cancellation of claims 2-8, 12-17, and 19-22.

**[19]** The rejection of claim 1-8, 12-13, 14 (claim 15 rejected as being dependent therefrom) 16-17, and 19-22 as being indefinite in the recitation of "RRF protein" (§ [9] part [e] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to claim 1 and cancellation of claims 2-8, 12-17, and 19-22.

***Claim Rejections - 35 USC § 101***

**[20]** The rejections of claim 1-8, 12-17, and 19-22 under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph, as not being supported by either a specific and substantial asserted utility or well-established utility (§§ [10] and [11] of the Office action mailed

9/16/2004) are withdrawn in view of applicants' argument and cancellation of claims 2-8, 12-17, and 19-22.

RESPONSE TO ARGUMENT: Applicants argue RRF is an essential protein and any inhibitor of RRF functions as an antibiotic, citing Janosi et al. (cited as reference C32 in the IDS filed 3/3/12/2002). Applicants point out assertions of use in the specification at pp. 1. and 6.

Applicants' argument is persuasive. The utility of the claimed method depends on the utility of the candidate compounds identified as a result of the screening methods (see p. 71, middle of the "Report on comparative study on protein 3-dimensional (3-D) structure related claims" of the "Trilateral Project WM4 Comparative studies in new technologies"). The reference of Janosi et al., supra, indicates that in vivo inactivation of RRF is bactericidal to *E. coli*, of which certain strains are known to be pathogenic and applicants assert that an inhibitor identified by the claimed method would function as an antibiotic. In view of applicants' argument, it is the examiner's position that the asserted utility of the claimed method for identifying compounds that can be used as antibiotics is substantial and specific.

***Claim Rejections - 35 USC § 112, First Paragraph***

[21] Claims 52-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims." In the claim amendments filed 2/18/2005 and 3/7/2005, applicants make no attempt to "show support" for the amendments as required by MPEP § 2163. In the interest of advancing prosecution, the examiner has unsuccessfully made an attempt to find support for the limitations of claims 52-59 in the specification, claims, and drawings as originally filed. MPEP § 2163 further states, "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description." As the examiner was unable to find support in the specification for the claims, a new matter rejection has been raised. It is suggested that applicants "show support" for the claimed limitations in accordance with MPEP § 2163.

**[22]** The written description rejection of original claims 1-8, 12-17, and 19-22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (¶ [12] of the Office action mailed 9/16/2004) is withdrawn in view of the amendment to the claims. Claims 2-8, 12-17, and 19-22 have been canceled, thus obviating the rejection of these claims. Claim 1 has been amended to limit the structure of the RRF protein to the "RRF protein according to Table 8." Table 8 discloses the amino acid sequence and the atomic coordinates of a crystallized RRF polypeptide of SEQ ID NO:1. In view of this amendment, it is the examiner's position that claim 1 and new



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claims 52-59, which depend therefrom, satisfy the written description requirement of 35 U.S.C. 112, first paragraph.

**[23]** The scope of enablement rejection of claims 1 and 52-59 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement (§ [13] of the Office action mailed 9/16/2004) is maintained for the reasons of record and the reasons stated below.

**RESPONSE TO ARGUMENT:** Applicants argue the claims have been amended to recite specific structural coordinates and in combination with the disclosure of the specification this enables a skilled artisan to practice the claimed invention. Applicants note that the claim uses “similar language” as US Patent 5,856,116.

Applicants' argument is not found persuasive. The examiner maintains the position that the specification fails to enable the claimed invention. While it is acknowledged that claim 1 has been amended to limit the three-dimensional structure of the RRF protein to having the amino acid sequence and atomic structural coordinates as defined in Table 8. However, this amendment fails to remedy the lack of guidance and working examples in the specification and the associated high level of unpredictability.

Applicants cite US Patent 5,856,116, as allegedly using language that is similar to the claims of the instant application. However, while the claim language may be of similar format, the disclosure of the instant application and that of the patent are markedly different. The disclosure of US Patent 5,856,116 teaches a working example of a three-dimensional structure of ICE *in complex with an inhibitor* (columns 16-18) and

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discloses the active site and accessory binding site amino acids of ICE (column 9) such that a skilled artisan could use, for example, molecular replacement or a three-dimensional representation of the disclosed active site amino acids to design an ICE binding compound *in silico*. Contrast the disclosure of the '116 patent to that of the instant application, which discloses the three-dimensional structure of an unliganded RRF protein and only speculates that one of Arg110, Arg129, or Arg132 may be an active site residue (p. 11). Moreover, it is noted that the method designs or selects binding compounds by any method, i.e., the claimed method is not limited to identifying those compounds that bind, e.g., the active site of RRF. Even if the claims were so limited, as noted in the previous Office action and undisputed by applicants, without knowledge of a protein's binding pocket, it must first be identified prior to design of binding compounds. While computer programs for *predicting* a protein's binding pocket exist, there is no reliable measure of the accuracy of such programs in selecting the correct binding pocket and as a result, such programs are likely to select multiple binding pockets. Thus, there is a high level of unpredictability in designing a binding compound as encompassed by the claims. In this case, it is not routine in the art to design a binding compound without knowledge of its binding pocket.

Also, it is noted that the claims are drawn to a method for identifying a compound capable of binding to RRF using a 3-D structure of RRF defined by the atomic structural coordinates of Table 8. The specification discloses only *computational* methods for identifying compounds that bind to RRF. However, the claims encompass both those methods that are computationally based in addition to those methods that are non-

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computationally based, e.g., using a ball-and-stick model of RRF to design binding compounds. However, the specification fails to provide any guidance or a working example of such a method and for reasons stated above, the method using such a ball-and-stick model for identifying binding compounds would be highly unpredictable. Further, such methods using a ball-and-stick model of a full-length protein are not typically practiced in the art and, while methods of creating 3-D structures of small molecules are routinely practiced in the art, it is not routine in the art to make a 3-D ball-and-stick representation of a full-length, 185 amino acid polypeptide for design of binding compounds.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**[24]** Upon further consideration following review of MPEP 2106 and Cases 6-7 of the "Report on comparative study on protein 3-dimensional (3-D) structure related claims" of the "Trilateral Project WM4 Comparative studies in new technologies," the following new rejection is deemed necessary.

**[25]** Claim(s) 1 and 52-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al. (US Patent 5,856,116; cited in the IDS filed 2/18/2005) in view In re

Gulack 217 USPQ 401 (Fed. Cir. 1983). The claims are drawn to a method for identifying a compound capable of binding to RRF using a three-dimensional structure of RRF as defined by the atomic structural coordinates of Table 8.

The reference of Wilson et al. teaches methods of designing and selecting compounds that bind to an enzyme using a three-dimensional model of said enzyme (columns 9-13 and claim 1). Wilson et al. teaches that the compound can be designed de novo or by using the structure of a known compound capable of binding to the enzyme (column 12, top and claims 2 and 3). Wilson et al. teaches steps for determining the bioactivity of the compound, e.g., synthesizing the compound and determining its effect on the enzyme (claim 1, steps c and d). The method as taught by Wilson et al. is the claimed method, only missing the specific structural coordinates as disclosed in Table 8.

In Gulack, the court held that nonfunctional descriptive material in a claim does not distinguish the prior art in terms of patentability. The key factor in analyzing the obviousness of these claims over the prior art is the determination that the computer algorithm used to identify compounds that may bind RRF is a known algorithm and is unmodified. If the difference between the prior art and the claimed invention as a whole is limited to descriptive material stored on or employed by a machine, it is necessary to determine whether the descriptive material is functional descriptive material or nonfunctional descriptive material. In this case, the RRF structural coordinates as disclosed in Table 8 are non-functional descriptive material and the method uses a known unmodified computer algorithm. Data, which are fed into a known algorithm

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whose purpose is to compare or modify those data using a series of processing steps, do not impose a change in the processing steps and are thus nonfunctional descriptive material. A method of using a known comparator for its known purpose to compare data sets does not become nonobvious merely because new data becomes available for analysis. Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to perform rational drug design as taught by Wilson et al. to identify a compound that binds to RRF, wherein only nonfunctional descriptive material is additionally present in the claims, which do not distinguish the claimed methods from Wilson et al. according to In re Gulack.

### ***Conclusion***

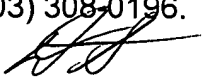
**[26]** Status of the claims:

Claims 1 and 52-59 are pending.

Claims 1 and 52-59 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Thursday and alternate Fridays from 7:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (571) 273-8300. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.



DAVID J. STEADMAN, PH.D.  
PRIMARY EXAMINER